REMARKS

Claims 1-52 remain pending.

Claim Rejection: 35 U.S.C. §112, second paragraph

Claims 15 – 30, 36 and 37 were rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claim 15 has been amended to remove the term "cytoplasm." Claims 36 and 37 have been amended so as to address any indefiniteness of the claims. Reconsideration of this rejection is requested.

Claim Rejection: Rejection under 35 U.S.C. §102

Claims 1-3, 5-9, 11, 15-17, 19-25, 30-32 and 35-39 were rejected under 35 U.S.C. 102(b) as being anticipated by Vogel et. al.

Anticipation can be found only if a reference shows exactly what is claimed. *Titanium Metals Corp. v. Banner*, 778 F.2d 775, 227 USPQ 773 (Fed. Cir. 1985). Anticipation requires identity of the claimed process and a process of the prior art; the claimed process, including each step thereof, must be described or embodied in a single reference. *Glaverbel Societe Anonyme v. Northlake Marketing & Supply, Inc.*, 45 F.3d 1550, 22 USPQ2d 1496 (Fed. Cir. 1995).

Vogel et al. is an improper 102 reference of the claims as amended.

Vogel et al. discloses an intravenous solution of photoactivatable porphycene dyes and additional solvents and adjuvants. Col. 11., Lines 45 – 47. When the intravenous solution is be dispensed from multiple dose containers, antimicrobial agents in bacteriostatic or fungistatic concentrations must be added. Col. 12, Lines 41 – 43. Among the compounds and concentrations used an antimicrobial agent is benzalkonium chloride (0.01%). Col. 12, Line 46.. Vogel et al. discloses the use of benzalkonium chloride with the porphycene compound, but only in the context of the known use of benzalkonium chloride, that of a bactericidal agent. Benzalkonium chloride is used to prevent bacterial or fungal growth which may occur as a result

of repeated extraction of porphycene compound from the multiple dose container. Vogel does not disclose the use of benzalkonium chloride to disrupt the membrane of a cell thereby allowing photosensitive agents to enter the cell. That Vogel et al. uses benzalkonium chloride as an antimicrobial agent is not unexpected, as benzalkonium chloride is a well known medical disinfectant.

Vogel also discloses the use of surfactants with porphycene in the formulation of a topically applied compounds. The surfactants are used to improving the viscosity of the gel.

The anticipation rejection based on Vogel et al. is improper for the following reasons:

– Vogel does not disclose the mechanism of passing photosensitive material into the cell interior, i.e., by applying benzalkonium chloride to compromise a cell membrane so as to permit the photosensitive material to diffuse into the cell interior, or

– Vogel does not disclose a topical application, surface release, inhalation, or intravenous or subcutaneous injection of benzalkonium chloride wherein the concentration of benzalkonium chloride is within the 0.001% to 1% range at the cell site. An intravenous administration of the Vogel would not result in a benzalkonium chloride concentration at a cell site within this range as the solution wold be effectively diluted within the volume of patient blood.

In light of the amendments above, it is suggested that claims 1-3, 5-9, 11, 15-17, 19-25, 30-32, and 35-39 are not anticipated by Vogel et al. As such, we respectfully request that the rejections based thereon be withdrawn.

Claim Rejection: Rejection under 35 U.S.C. §103

Claims 1, 4, 15, 18, 31, 33-35, and 40-52 were rejected under 35 U.S.C. §103(a) as being unpatentable over Wilk et al., in view of Vogel et al. The Examiner stated:

> Wilk et al teach sterilizing equipment such as catheters using light applied internally or externally of the surface and the use of a sterilizing solution. Vogel et al teach a solution as claimed that can be used in conjunction with light to kill bacteria or to treat viral conditions. Paper 4, Page 2.

It is submitted that this interpretation of Wilk et al. is flawed as this reference does not disclose the use of a sterilizing solution to one of ordinary skill in the art.

While Wilk et al. does disclose the use of a saline solution flush during a sterilization process, it does not teach the use of a "sterilizing solution". Saline solution is not a "sterilizing solution" to one of ordinary skill in the art. The saline solution of Wilk et al. is provided to ensure electrical conductivity of the solution. As saline solution has no antimicrobial properties, such a solution is not a "sterilizing solution" as suggested by the Examiner.

Furthermore, there is no teaching or suggestion to replace the intravenous solution disclosed in Vogel with the saline solution in Wilk. The Examiner is simply engaging in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps, an activity the Federal Circuit has repeatedly indicated as improper. *In re Gorman*, 933 F.2d 982, 19 USPQ2d 1885 (Fed. Cir. 1991). There must be some reason for the combination other than the hindsight obtained from the invention itself. *Interconnect Corp. v. Ultraseal Ltd.*, 781 F.2d 861, 228 USPQ 90 (Fed. Cir. 1985). The Examiner has not established a prima facie case of obviousness by failing to provide the motivation or reasoning as to why the combination of references is proper.

Furthermore, as additional support to the nonobviousness of the present invention, we have attached a product listing sheet and a published article on benzalkonium chloride. Both publications state that benzalkonium chloride is unacceptable sterilant of medical equipment. Similarly, data in FIGS. 2 and 3 suggest that benzalkonium chloride is an ineffective sterilant. It is only through the novel method employed in the present invention that benzalkonium chloride can be effectively used in a sterilization process for medical equipment. An unexpected result of the present invention is that a photodynamic therapy using benzalkonium chloride is effective against a broad spectrum of organisms including gram positive and gram negative bacteria, funguses, viruses, spores and cancer cells.

We submit that the present invention as currently claimed is not made obvious by the combination of Wilk and Vogel. Consequently, we respectfully request that the rejections based thereon be withdrawn.

Claim Rejection: Rejection under 35 U.S.C. §103

Claims 1, 5, 10, 12-15, 20 and 26-29 were rejected under 35 U.S.C. §103(a) as being unpatentable over Vogel et al., in view of Nitzan et al. The Examiner stated:

> "Vogel et al teach a method of eradicating acellular or cellular organisms as claimed but does not teach adding the surface acting agent prior to the photosensitive material, or a plurality of photosensitive or surface acting agents or the light dosage rate." Paper 4, Page 3.

It is respectfully submitted that Vogel does not teach a method as claimed except for the adding the surface acting agent prior to the photosensitive material, or a plurality of photosensitive or surface acting agents or the light dose rate. Vogel does not teach or suggest the mechanism of introducing photosensitive material into a cell interior by application of benzalkonium chloride to compromise a cell membrane.

The Examiner further stated:

> "Nitzan et al teach a method as claimed (The PMNP, which is made from Polymyxin B sulfate, will retain some of amount of Polymyxin B sulfate therein, and thus is considered a mixture of a plurality of surfactants) except for the specific time period between the addition of the two agents and the use of benzalkonium chloride." Paper 4, Page 3.

Nitzan et al does not disclose, teach, or suggest the method as claimed except for the specific time period between the addition of the two agents and the use of benzalkonium. Nitzan teaches the use of polycationic agent polymyxin nonapeptide (PMNP) and the photosensitizer deuteroporphyrin (DP) to eradicate the gram negative bacteria E Coli and Pseudomonas aerugenosa. Nitzan uses the PMNP to bind the PMNP-DP complex to the cell membrane, much as a membrane specific antibody would. Neither PMNP or the PMNP-DP complex cause a disruption of the cell membrane (pp 94 1st column). Unlike the present invention, Nitzan teaches the use of a surfactant to assist in the binding of the photosensitizer to the cell membrane exterior. Nitzan does not disclose or suggest passing a photosensitizer through a surfactant-compromised cell membrane. Nitzan teaches away from the concept of using photosensitizers

and a surfactant such as benzalkonium chloride to increase the cell membrane permeability and allow the photosensitizer to enter the cell by diffusion as is disclosed in the present invention.

There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the art would make the combination to achieve the subject matter of the present claims. *See*, Symbol Technologies, Inc. v. Opticon Inc., 935 F.2d 1569, 19 USPQ2d 1241 (Fed. Cir. 1991). Since no such reason, suggestion or motivation exists, the pending claims are not obvious in view of the known prior art.

Even assuming that the combination of Vogel and Nitzan as proposed by the Examiner was proper, the combination of references would fail to disclose or teach the invention as presently claimed, i.e., improved photodynamic cellular disruption by the mechanism of introducing a photosensitive material into a cell interior via diffusion through a benzalkonium chloride compromised cell membrane. As such, the claims as amended are not made obvious in light of the cited references. Consequently, we respectfully request that the rejection based on Vogel and Nitzan be withdrawn.

Demand for Documentary Proof

Nitzan et al. discloses use of a purified polymyxin nanapeptide preparation –PMNP. (p. 90). PMNP is a derivative of polymyxin B, and each compound has unique properties relative to the other. Polymyxin B is a relatively toxic antibiotic. PMNP is less toxic than polymyxin B and is devoid of antibiotic activity. The toxicity of polymyxin B limits its potential as a therapeutic agent.

The Examiner continues to allege that purified PMNP will retain some amount of Polymyxin B sulfate therein. The applicant traverses such an assertion. Pursuant to M.P.E.P. 2144.02 -.03, the applicant demands that evidence supporting the Examiner's position be provided.

The rationale to support a rejection under 35 U.S.C. 103 should rely on logic and sound scientific principle. *In re Soli*, 317 F2d 941, 137 USPQ 797 (CCPA 1963). When the Examiner relies on a scientific theory, evidentiary support for the existence and meaning of that theory must be provided. *In re Grose*, 592 F2d 1161, 201 USPQ 57 (CCPA) 1979.

CONCLUSION

Applicant respectfully requests that the Examiner reconsider the pending claims. Please direct any questions regarding this application to John Klos at (612) 321-2806.

Respectfully submitted,
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CERTIFICATE OF FACSIMILE TRANSMISSION UNDER 37 C.F.R. 1.8:
I hereby certify that this paper and any papers referred to herein are being sent via facsimile to Commissioner for Patents telephone number 703-872-9302 on June 27, 2003.

John F. Klos:
Signature